DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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April 3, 2002

Richard M. Cagen
Administrator
LDS Hospital
Eighth Avenue and C Street
Salt Lake City, UT 84143

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1089

Research Project: **Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Respiratory Distress Syndrome. (N Engl J Med 2000; 342:1301-8)**
Project Title: **Prospective, Randomized, Multicenter Trial of 12 ml/kg vs 6 ml/kg Tidal Volume Positive Pressure Ventilation and Ketoconazole vs Placebo fro the Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome**
Principal Investigator: Alan H. Morris, M.D.
IRB Number: **IRB# 617**
HHS Project Number: N01-HR46063

Dear Mr. Cagen:

The Office for Human Research Protections (OHRP) has reviewed the LDS Hospital's March 1, 2002 report that was submitted in response to OHRP's February 4, 2002 letter regarding the above-referenced research.

Based upon its review, OHRP makes the following determinations regarding the above-referenced

research:

(1) In its February 4, 2002 letter, OHRP found that the informed consent documents reviewed by the LDS Hospital Institutional Review Board (IRB) failed to adequately describe the reasonably foreseeable risks and discomforts of the research, as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(a)(2).

Corrective Action: LDS Hospital has committed to continuing a strong relationship between its investigators and the IRB to ensure the ethical conduct of research. LDS Hospital has also revised its review form for new research to allow for greater detail in the review by the primary reviewer and the IRB. OHRP finds that these corrective actions adequately address the finding in OHRP's February 4, 2002 letter.

(2) HHS regulations at 45 CFR 46.111(b) stipulate that in order to approve research, the IRB shall determine that when some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of the subjects. In its February 4, 2002 letter, OHRP expressed concern that the LDS Hospital IRB may have failed to ensure that this requirement was satisfied for the above referenced research.

OHRP finds that LDS Hospital has adequately addressed this concern. Furthermore, OHRP acknowledges that LDS Hospital has implemented procedures to ensure that additional safeguards are included in research involving subjects who may be vulnerable to coercion or undue influence.

(3) OHRP finds that LDS Hospital ha adequately addressed the additional concerns raised in OHRP's February 4, 2002 letter.

As a result of the above determinations, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Patrick J. McNeilly, Ph.D.

Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Mr. David Grauer, LDS Hospital
Dr. A. Jennifer Fishbach, IRB Chair, LDS Hospital
Dr. Alan Morris, LDS Hospital
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. George Gasparis, OHRP
Ms. Jan Walden, OHRP
Mr. Barry Bowman, OHRP